In the Specification

Please amend paragraph 0001 as follows:

This is a continuation application of U.S. Pat. Application Serial No. 09/990,531, filed November 21, 2001, now allowed, which is a continuation-in-part application of U.S. Pat. Application Serial No. 09/870,433, filed May 29, 2001, which is a continuation application of U.S. Pat. Application Serial No. 09/660,877, filed September 13, 2000, now U.S. Patent No. 6,251,639 B1, which claims the priority benefit of provisional patent applications U.S. Serial No. 60/153,604, filed September 13, 1999, and U.S. Serial no. 60/175,780, filed January 12, 2000, all of which are incorporated by reference in their entirety.

Please amend paragraph 0005 as follows:

The detection of sequence alterations in a nucleic acid sequence is important for the detection of mutant genotypes, as relevant for genetic analysis, the detection of mutations leading to drug resistance, pharmacogenomics, etc. Various methods for the detection of specific mutations include allele specific primer extension, allele specific probe ligation, and differential probe hybridization. See, for example, U.S. Patent Nos. 5,888,819; 6,004,744; 5,882,867; 5,710,028; 6,027,889; 6,004,745; and PCT Publication No. WO ~~US~~88/02746. Methods for the detection of the presence of sequence alterations in a define nucleic acid sequence, without the specific knowledge of the alteration, were also described. Some of these methods are based on the detection of mismatches formed by hybridization of a test amplification product to a reference amplification product. The presence of mismatches in such hetero-duplexes can be detected by the use of mismatch specific binding proteins, or by chemical or enzymatic cleavage of the mismatch. A method for detection of sequence alteration which is based on the inhibition of branch migration in cruciform four stranded DNA structures was recently described. See, for example, Lishanski, A. et al. *Nucleic Acids Res* 28(9):E42 (2000). Other methods are based on the detection of specific conformations of single stranded amplification products. The secondary structure of a single stranded DNA or RNA is dependent on the specific sequence. Sequence alterations in a test nucleic

acid target relative to a reference sequence leads to altered conformation. Altered conformation of a single stranded amplification product can be detected by a change in the electrophoretic mobility of the test amplification product as compared to that of a reference amplification product. Single stranded conformation polymorphism, SSCP, is widely used for the detection of sequence alterations. See, for example, Orita M., et al. *Proc Natl Acad Sci U S A* 86(8):2766-70 (1989); Suzuki, Y. et al. *Oncogene* 5(7):1037-43 (1990); and U.S. Patent No. 5,871,697. This method is also used in microbial identification that is based on the defined changes in a specific nucleic acid sequence in different strains or species. Mutation detection using the SSCP methods mostly employs DNA amplification products, however, RNA-SSCP methods have also been described. Sequence dependent conformation of a single stranded RNA is well-documented and was shown to lead to a defined electrophoretic mobility pattern. See, for example, Sarkar et al. *Nucleic Acid Research* 20(4):871-878 (1992) and Gasparini et al. *Hum. Genet.* 97:492-495 (1996).

Please amend paragraph 0138 as follows:

DNA polymerases for use in the methods and compositions of the present invention are capable of effecting extension of the composite primer according to the methods of the present invention. Accordingly, a preferred polymerase is one that is capable of extending a nucleic acid primer along a nucleic acid template that is comprised at least predominantly of deoxynucleotides. The polymerase should be able to displace a nucleic acid strand from the polynucleotide to which the displaced strand is bound, and, generally, the more strand displacement capability the polymerase exhibits (i.e., compared to other polymerases which do not have as much strand displacement capability) is preferable. Preferably, the DNA polymerase has high affinity for binding at the 3'-end of an oligonucleotide hybridized to a nucleic acid strand. Preferably, the DNA polymerase does not possess substantial nicking activity. Preferably, the polymerase has little or no 5'->3' exonuclease activity so as to minimize degradation of primer, termination or primer extension polynucleotides. Generally, this exonuclease activity is dependent on factors such as pH, salt concentration, whether the template is double stranded or single stranded, and so forth, all of which are familiar to one skilled in the art. Mutant DNA polymerases in which the 5'->3' exonuclease activity has been deleted, are known in the art and are suitable for the amplification

methods described herein. Suitable DNA polymerases for use in the methods and compositions of the present invention include those disclosed in U.S. Pat. Nos. ~~5648211~~5,648,211 and ~~5744312~~5,744,312, which include exo$^-$ Vent (New England Biolabs), exo$^-$ Deep Vent (New England Biolabs), Bst (BioRad), exo$^-$ Pfu (Stratagene), Bca (Panvera), sequencing grade Taq (Promega), and thermostable DNA polymerases from thermoanaerobacter thermohydrosulfuricus. It is preferred that the DNA polymerase displaces primer extension products from the template nucleic acid in at least about 25%, more preferably at least about 50%, even more preferably at least about 75%, and most preferably at least about 90%, of the incidence of contact between the polymerase and the 5' end of the primer extension product. In some embodiments, the use of thermostable DNA polymerases with strand displacement activity is preferred. Such polymerases are known in the art, such as described in U.S. Pat. No. ~~5744312~~5,744,312 (and references cited therein). Preferably, the DNA polymerase has little to no proofreading activity.

Please amend paragraph 0217 as follows:

Amplification products can also be used for detecting whether or not a nucleic acid sequence of interest is present in a sample. For example, presence of a nucleic acid sequence of interest in a sample can be detected by detecting the sequence of interest in amplification product resulting from amplifying polynucleotides in a sample suspected of comprising the sequence of interest. As would be evident to one skilled in the art, detection of the complement of a sequence of interest in an amplification product can also be deemed to be indicative of the presence of the sequence of interest in a sample; conversely, absence of the complement of the sequence of interest would be indicative of absence of the sequence of interest in a sample. In some embodiments, a sequence of interest comprises a mutation, for example, a single nucleotide polymorphism, an insertion, a deletion or a substitution. A sequence of interest (or its complement) in an amplification product can be detected by any of a variety of methods known in the art, including, for example, hybridizing amplification product comprising (or suspected of comprising) the sequence of interest (or its complement) with a nucleic acid probe that is hybridizable (e.g., hybridizes) to the sequence of interest (or its complement). Suitable nucleic acid probes would be evident to one skilled in the art, and include, for example, probes that comprise DNA, RNA, DNA and RNA, peptide nucleic

acid (PNA), or any combination of DNA, RNA and/or PNA. These probes can be provided in any suitable form, including, for example, as microarrays, which may comprise the probe immobilized on a suitable substrate that can be fabricated from a material such as paper, glass, plastic, polypropylene, nylon, polyacrylamide, nitrocellulose, silicon and optical fiber. Detection of sequence of interest in an amplification product can also be achieved by methods such as limited primer extension, which are known in the art and described in, for example, U.S. Patent Nos. 5,888,819; 6,004,744; 5,882,867; 5,710,028; 6,027,889; 6,004,745; 5,763,178; 5,011,769; 5,185,243; 4,876,187; 5,882,867; WO ~~US~~88/02746; WO 99/55912; WO_92/15712; WO 00/09745; WO 97/32040; WO 00/56925, and in co-pending U.S. Application Ser. No. 60/255,638, filed 13 December, 2000.